IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Andreas SEWING et al. : Group Art Unit: 1616

Serial No.: 09/885,287 : Examiner: Gollamudi S

Filed: June 21, 2001:

For: COATING FOR METALLIC IMPLANT MATERIALS

REPLY BRIEF UNDER 37 C.F.R.§ 41.41

MAIL STOP:
APPEAL BRIEF-PATENTS
Commissioner for Patents
Box 1450
Alexandria, Virginia 22313-1450

SIR:

In response to the Examiner's arguments presented in the Examiner's Answer dated 28 October 2008, the Appellants' submit the following comments:

Even if a skilled worker were motivated to combine the various features of the cited prior art, which they are not, they would not arrive at the coated implant of the present invention.

A) At page 6 of the Examiner's Answer, the Examiner continues to allege that Lussi et al. teaches that HA particles with the instant particle size resorb better and cause generation of new bone faster. (The hydroxyapatite crystals of the instant claims have a length of about 300 to 500 nm). She points to table 1 of Lussi. However, Table 1 of Lussi et al. summarizes the results of sample material, which were heated between 600°C and 800°C. Sample material that were heated to 700°C had a crystal size of approx. 100 to 300 nm and material that was heated to 800°C had a crystal size of approx. 100 to 400 nm. However, col. 3 lines 58-65 of Lussi et al. teaches:

> "The final and essential step in the treatment of the bone mineral consists of dry heating to temperatures between 250°C and 600°C, preferably not greater than 550°C, more preferably between 350°C and 500°C, for several hours. The higher temperatures are more effective in removing

> contaminants but tend to increase the risk of recrystallization with consequent increase of crystal size. Heating in an oxygen-enriched atmosphere promotes the beneficial oxidation of organic residues. "

The instant particle size is only taught in the context of 700-800°C temperatures and Lussi et al. teaches a skilled worker away from the use of such high temperatures because they tend to increase the risk of recrystallization. Furthermore, at col.1 lines 49-55, Lussi states:

> "It should be emphasized that bone mineral which has been subjected to a treatment which results in significant increase in crystal size is much less readily remodeled on implantation since osteoclasts and osteoblasts cannot readily perform on such large crystals the dual function of mineral resorption and generation of new bone. Such implanted inserts may thus remain unchanged indefinitely eventually giving rise to undesirable effects."

Thus, Lussi et al. emphasizes that treatment which results in significant increase in crystal size is much less readily remodeled and as noted above Lussi et al. teaches that particles created at 700-800°C increase the crystal size.

Lussi et al. would lead a skilled worker away from the present invention.

B) On page 5 of the Examiner's answer, the Examiner states: "...It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of JP and Constanz et al and further add collagen to the hydroxyapatite coating."

JP 11-047219 relates to an implant solely coated with highly crystalline hydroxyapatite. The coating is applied by plasma-spraying under increased temperatures (i.e., above 170°C) and pressure (see Examples). However, collagen is a protein which would simply denature at such high temperatures. Thus, it would not be possible to simultaneously precipitate collagen. The conditions applied in the plasma-spraying processing contradict the bone forming conditions in the human body (i.e., 37°C body temperature and normal pressure). Thus, a skilled worker would not consider using a plasma-spraying process in order to obtain a bone analogous coating.

A simple dipping of a hydroxyapatite coated implant according to JP11-047259 in a collagen solution as taught by Constanz et al. also

would not lead to the present bone-analogous coating. The FTIR spectra shown in Figure 1 and 2 of the Brief on Appeal very clearly depict the differences between the present coating and a coating obtained by a simple mixture of hydroxyapatite and collagen.

C) On page 13 of the Examiner's answer, the Examiner states: "It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Worch and Liu and utilize calcium phosphates."

Worch at al. (US 6,524,718) describes a metallic object with a polyphase oxide coating obtained by anodic polarization. In this process a metallic oxide phase on, the implant surface is formed followed by the incorporation of inorganic and/or organic component into the oxide phase such that the polyphase oxide coating compares with an alloy (see column 2, lines 55 – 59 of Worch et al.).

The differences between the Worch et al. implant and the present implant are striking. The present implant is coated with mineralized collagen obtained in a cathodic polarization process where the metallic implant functions as a cathode. The implant according to Worch et al. functions as an anode in an anodic polarization process. A skilled worker would recognize that an anodic process and a cathodic polarization would not achieve the same results.

Liu et al. teaches a simultaneous addition of calcium and phosphate to the collagen slurry and the formation of a collagen membrane. As can be seen in Examples 1 and 2, Liu at al. uses an excess of calcium ions (500 mM, 300 mM) and phosphate ions (500 mM, 372 mM). Under these conditions calcium phosphate precipitates immediately after the solutions are mixed.

Thus, a combination of Worsh et al. and Lui et al. would lead to a

process where 1) an anodic polarization process is applied to an implant which is immersed in 2) an oversaturated calcium phosphate solution comprising collagen in which calcium phosphate is already precipitated and thus no longer in solution. Therefore, calcium phosphate cannot precipitate on the implant surface.

D) On page 19 of the Examiner's answer, the Examiner states: "It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shirkanzadeh and Liu and utilize the instantly claimed calcium phosphates."

Shirkanzadeh et al. teaches an electrochemical process for the deposition of bioactive material made of calcium phosphate on metallic implants. However, the size of the calcium phosphate crystals formed on the implant surface is between 2 to 20 µm (2000 - 20,000 nm). Thus, the crystals are too large for the purpose of forming a mineralized collagen matrix. Applying hydroxyapatite crystals of a size that is much larger then the collagen fibrils would lead to a domination of the mineral component and a simple admixture of the collagen into the mineral matrix.

Thus, even if a skilled worker were to combine the teachings of Shirkanzadeh with Liu et al., they would not arrive at the present implant. As described above, by mixing a highly concentrated calcium and phosphate solution according to Liu et al. the calcium phosphate would immediately precipitate. Thus, the slow process of calcium phosphate formation on collagen fibrils which is required in order to form a mineralized collagen matrix that is constructed in the form of layers, whereby at least one of said layers comprises a composite of mineralized collagen fibrils, amorphous calcium phosphate and crystalline hydroxyapatite and the crystals of said crystalline hydroxyapatite have a length of about 300 to 500 nm would simply not be possible.

For the reasons provided above, reversal of the rejections under 35 U.S.C. §103 and the obviousness-type double patenting rejection are respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Brion Heaney/

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Brion Heaney, Reg. No. 32,542
Attorney/Agent for Applicant(s)

/Jennifer Branigan/

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Jennifer Branigan, Reg. No. 40,921
Agent for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

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